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(19)

(54) COLLAGENIC MEDICINAL DRESSING

(71) We, INTREPRINDEREA FLACARA ROSIE, a Rumanian corporate body of Str. Bella Brainer nr. 67—93, Bucarest, Rumania, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed to be particularly described in and by the following statement:—

This invention concerns a process for preparing a collagen-based material suitable for medicinal dressings.

Medicinal dressings comprising a collagen foam are known (U.K. specification No. 942226) and are used as skin plasters, particularly for burns.

There are various known processes for preparing the collagen foam. For example, in one process, a 1.2% collagen solution is homogenized and then introduced into a cylinder, the bottom of which is made of fritted glass, air or another inert gas being introduced into the cylinder under pressure. After foaming, the collagen is gelled with cadmium nitrate solution, which is then eliminated by washing. After drying, the resulting sheet is friable and, in use, is covered with another foil, also collagen-based which has a harder consistency and which may advantageously contain a bactericide or a bacteriostatic agent.

A disadvantage of this process is that it involves several steps and the collagen foam produced needs a hard foil cover which, in use, hinders the elimination of secretions from a wound.

Another method of making collagen dressings of a spongy consistency comprises freezing a collagen sol for at least about 12 hours at −20°C and then eliminating the water by means of a water-miscible organic solvent, which does not attack the collagen. Three or four successive extractions are required which together take about 8 hours. Thereafter, the product is air dried which can take 12 or more hours. The sponge obtained generally has a density of 0.015—0.6 g/cm³. This method while providing a good porosity spongy mass, takes a long time and includes several laborious steps.

Another process involved freezing an acid collagen sol and subliming the water under a high vacuum at a temperature below the freezing point. This process has the disadvantage that the product has a very large porosity.

We have now devised an improved process for making a collagen-based dressing material, which process is less laborious and time-consuming and provides an improved material. According to the invention, there is provided a process for preparing a collagen-based medicinal dressing material which comprises freezing a collagen polydispersion (as herein defined) to a temperature of −65°C or lower, the polydispersion being of concentration 0.66 to 2% collagen based on the weight of the polydispersion, and drying the frozen polydispersion by vacuum sublimation at a final temperature not exceeding 35°C.

In another aspect, the invention provides a process for preparing a collagen-based medicinal dressing material which comprises freezing a collagen polydispersion (as herein defined) obtained from cattle hide, by subjecting the polydispersion to a temperature of from −65°C to −70°C for from 2.5 to 3.2 hours, the polydispersion being of concentration 0.66 to 2% collagen based on the weight of the polydispersion, and drying the frozen polydispersion by subjecting it to vacuum sublimation at a pressure of 10^{-3} to 10^{-6} torr, for a period of from 24 to 48 hours and at a final temperature not exceeding 35°C.

By "collagen polydispersion" we mean a solution of collagen which is not an "ideal" solution, that is one containing only collagen molecules of molecular weight about 300,000, but rather is a solution in which the collagen molecules have varying molecular weights from about 95,000 up to about 1.5×10^6. Such polydispersions may be obtained by treating cattle hide to break the interfibrilary bonds and then totally dissolving the treated hide in a solvent. The polydispersions do not contain any solid dispersed particles of

collagen and the term "polydispersion" is used to indicate the properties of the dissolved collagen.

Preferably, the polydispersion contains a bactericide and/or a bacteriostatic agent.

In order that the invention may be more fully understood, the following Example is given by way of illustration only.

EXAMPLE

1000 ml of collagen polydispersion (0.8% concentration of collagen based on the weight of the polydispersion) in a 2% boric acid solution, and 0.1 g of sodium merthiolate (as bactericide), were placed in a mechanical stirrer and homogenized until the fibre agglomerations had disappeared. After perfect homogenization, the polydispersion was distributed into jars made of epoxy resins (which ensure a uniform heat exchange with the surrounding medium and to which the collagen solution does not adhere), the thickness of the layer inside the jars being 15mm.

The jars containing the collagen polydispersion were introduced into a freezer in which the temperature was between −65°C and −70°C and left for 2.5 to 3.2 hours (in view of the uniformization of the crystal structure of the ice). After this time, the frozen solvent was sublimed under a vacuum of 10^{-3} to 10^{-5} torr, at an initial temperature of −40°C to −50°C. The duration of the sublimation process was 30 hours, the final temperature not being allowed to exceed +35°C.

A spongy collagenic material was obtained which was white, elastic, compressible, easy to mould, fine-pored and had a density of 0.03 to 0.06 g/cm³.

The material was removed from the jars and put into polyethylene bags. The bags were closed and sterilized (by irradiation with gamma rays or otherwise).

With a view to accelerating the healing of wounds and for maintaining sterility, various medicinal bactericides or bacteriostatic agents may be added to the homogenous collagen poly-dispersion before freezing. Thus, for example, tetracycline may be added in an amount of 0.5 to 2 g per 1000 ml of polydispersion and/or hydrocortisone in an amount of 0.5 to 0.75 g per 1000 ml of polydispersion.

The dressing material made by the method of the invention has good capillarity and is of wide applicability.

WHAT WE CLAIM IS:—

1. A process for preparing a collagen-based medicinal dressing material which comprises freezing a collagen polydispersion (as herein defined) to a temperature of −65°C or lower, the polydispersion being of concentration 0.66 to 2% collagen by weight of the polydispersion, and drying the frozen polydispersion by vacuum sublimation at a final temperature not exceeding 35°C.

2. A process for preparing a collagen-based medicinal dressing material which comprises freezing a collagen polydispersion (as herein defined) obtained from cattle hide, by subjecting the polydispersion to a temperature of from −65°C to −70°C for from 2.5 to 3.2 hours, the polydispersion being of concentration 0.66 to 2% collagen by weight of the polydispersion, and drying the frozen polydispersion by subjecting it to a vacuum sublimation at a pressure of 10^{-3} to 10^{-5} torr, for a period of from 24 to 48 hours and at a final temperature not exceeding 35°C.

3. A process according to claim 1, wherein the polydispersion contains a bactericide and/or a bacteriostatic agent.

4. A process according to claim 2 wherein the polydispersion contains a bactericide and/or a bacteriostatic agent.

5. A process for preparing a collagen-based medicinal dressing material substantially as herein described in the Example.

6. A collagen-based medicinal dressing material produced by the process of claim 1.

7. A collagen-based medicinal dressing material produced by the method of claim 2, 4 or 5.

8. A medicinal dressing comprising a material as claimed in claim 6.

9. A medicinal dressing comprising a material as claimed in claim 7.

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